in rats transfected with the HGF gene compared with control vector at 4 weeks after transfection.

**Conclusion:** Overall, those results may indicate that the effect of angiogenesis by local transfected HGF gene is not at least through the NO. Furthermore, transfected HGF gene may have the effect of angiogenesis in the several conditions of impaired NO synthesis.

1178-144 **In Vivo Electroporation of Hepatocyte Growth Factor Gene Into Skeletal Muscle of a Cardiomyopathic Hamster Ameliorates Cardiac Dysfunction and Fibrosis**

Yuko Tsujita, Kazuo Komamura, Masafumi Kitakaze, Kunio Miyatake, National Cardiovascular Center, Osaka, Japan

**Background:** Hepatocyte growth factor (HGF) has potent angiogenesis and antifibrosis effects. We examined whether the electroporation of HGF gene into skeletal muscle of dilated cardiomyopathy hamster could affect on cardiac function and fibrosis. **Methods** Plasmid vector expressing HGF (800 mcg) was transfected into the bilateral tibialis anterior muscles of 12 TO-2 hamsters of 11 weeks of age by electroporation once a week up to 14 weeks of age. Empty plasmid was transfected into other 12 hamsters. Echocardiographical, hemodynamic, histopathological and biochemical changes were measured before and after electroporation. **Results:** Electroporation increased the serum HGF levels to >10ng/mL in treated hamsters, whereas control hamsters showed no increase. LV ejection fraction (47.9+/-9.4 vs. 28.8+/-11.2 %, p<0.01), and E/A ratio (1.24+/-0.33 vs. 3.99+/-1.01%, p<0.05) were better in treated hamsters than in control hamsters. Systemic vascular resistance (3.31+/-1.30 vs. 7.34+/-4.99 mmHgmin/mL) was lower in treated hamsters than in control hamsters. Although left ventricular weight to tibialis length ratio (12.6+/-1.2 vs. 12.9+/-1.2 mg/g, NS) was similar, area of fibrosis in the ventricles (11.8+/-3.4 vs. 17.8+/-3.5 %, p<0.05) and hydroxyproline content (3.7+/-0.7 vs. 5.1+/-0.9 mmol/g, p<0.01) were less in treated hamsters than in control hamsters. Capillary density (1885+/-232 vs. 1447+/-182 vessel/mm2, p<0.01) was higher in treated hamsters than in control hamsters. **Conclusion:** These findings suggest that HGF gene transfer into muscle by electroporation is an effective means of delivery of HGF for treatment of heart failure due to dilated cardiomyopathy.

1178-145 **Transfection With DNA of Soluble VCAM-1 Causes Monocyte Chemotaxis and Increased Endothelial Cell Staining: A New Gene-Therapeutic Approach for Angiogenesis?**

Mirjam Decker, Uta Weirich, Thomas Nordt, Simone Bauer, Joerg Kreuzer, Christoph Bode, Karlheinz Peter, University of Freiburg, Freiburg, Germany

**Background:** Monocytes have been described as local mediators of angiogenesis. For monocyte recruitment, chemotaxis and adhesion to endothelial cells are major prerequisites. We hypothesized that soluble parts of endothelial adhesion molecules act as chemotactic factors and thereby may promote angiogenesis.

**Methods and Results:** Soluble (s) Adhesion molecules were tested for chemotactic activity using the monocytic cell line U937 in a 48-well microchemotaxis chamber. Only sVCAM-1, but not sICAM-1, or sE-selectin exhibited a significant concentration-dependent chemotactic effect at concentrations between 10 to 675nM. To test for a potential angiogenic effect of sVCAM-1, we designed an expression vector of a truncated form of the VCAM-1 gene encoding for sVCAM-1. After thoracotomy, rats were injected intramyocardially with naked sVCAM-1-DNA into the left ventricle. 21 days later, hearts were stained for macrophages with an ED1 antibody and for endothelial cells with indoxyl-tetrazolium (IT). Injection of sVCAM-1 DNA (n=10) results in 3.7±1.1% of ED1 positive area (area without injection (control, n=5): 0.03±0.02%, p<0.001) and in 8.5±2.2% of IT positive area (control: 5.1±0.9%, p<0.001). Injection controls with PBS (n=10), and the βGal gene (n=10) did not reveal statistically significant differences in macrophage and endothelial cell staining.

**Conclusions:** Transfection of soluble-VCAM-1-DNA induces chemotaxis on monocytes and causes an increase in endothelial cell staining in rat hearts. Further studies are warranted to prove that the transfer of soluble-VCAM-1-DNA represents a potential gene therapeutic approach for angiogenesis.

POSTER SESSION

## 1179 Vascular Mechanics

Tuesday, April 01, 2003, Noon-2:00 p.m.
McCormick Place, Hall A
Presentation Hour: 1:00 p.m.-2:00 p.m.

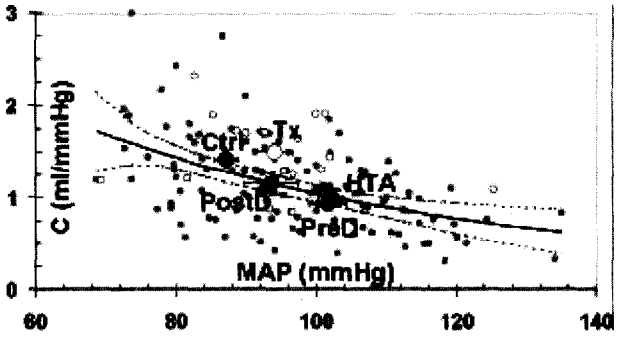
1179-146 **More Favorable Improvement of Arterial Wall Characteristics by Renal Transplantation Than by Hemodialysis**

Tine L. de Backer, Stephane G. Carlier, Brian A. Haluska, Patrick Segers, Han-Yo E. Ie, Thomas H. Marwick, Cardiovascular Center OLV Ziekenhuis, Aalst, Belgium, University of Queensland, Brisbane, Australia

**Background:** End stage renal disease is associated with reduced arterial compliance (C) and increased cardiovascular events. We evaluated C following hemodialysis (D) and renal transplantation (Tx).

**Methods:** Measurements were done in 32 controls(Ctrl, mean age 43y), 43 hypertensives(HT,58y), 18 D(58y) and 18 Tx pts matched to D for age and sex. Central pressure was derived by radial applanation tonometry using a transfer function. Aortic(Ao) flow was simultaneously measured with Doppler. C was evaluated by the pulse pressure method, an iterative search of the best fit between measured Ao pulse pressure and pulse pressure predicted by a 2-element Windkessel. In D pts recordings were done 1 hr before and 1 hr after dialysis.

**Results:** HT and preD had a significantly (p<0.05) higher mean arterial pressure (MAP) than Ctrl, postD and Tx. This led to significantly lower C for HT and preD (1.00±0.38 and 0.94±0.34), vs Ctrl, post D and Tx (1.42±0.54, 1.15±0.54, 1.49±0.40 ml/mmHg, respectively). After accounting for differences in MAP, Ctrl, HT, pre and post D values could all (•, graphic) be predicted by the same Langewouters' model(line and 95% CI). However, Tx(°) demonstrated supra-normal values of C for a MAP(94±11 mmHg) similar to postD but a pulse pressure (49±15 mmHg) similar to Ctrl.




**Conclusion:** Improvement of compliance after dialysis follows the non-linear Langewouters' pressure-volume relationship. Renal Tx improves arterial wall characteristics to a higher degree that may be related to structural changes.

1179-147 **Mental Stress Inhibits the Intimal Fibromuscular Proliferation Through Endogenous Opioid System in the Process of Arterial Remodeling**

Kunimitsu Iwai, Masayuki Matsumoto, Kenichi Kawanishi, Yukiharu Nishimura, Hiroshi Murai, Ling Y. Kong, Tsuyoshi Nakahashi, Hideyuki Hattori, Shigeto Morimoto, Kanazawa Medical University, Ishikawa-ken, Japan

**Purpose** Mental stress is speculated to be the trigger for the rupture of fibrous cap around the coronary arteriscleratic plaque. We investigated the influence of mental stress on the intimal fibromuscular proliferation in the rat model of arterial remodeling after endothelial injury in connection with two stress hormone systems. **Methos and Results** In Wister-Kyoto rats (eight groups,each:n=10) the endothelium of abdomial aorta was denuded with balloon catheter. (1)denudation (2)denudation + immobilization(6hrs/d) (3)denudation + naltolexone (NAL:2mg/kg/d ip) (4)denudation + NAL + immobilization (5)denudation + beta-endorphin(END:10ng/kg/d ip) (6)denudation + NAL + END (7) denudation + phentolamine(10ng/kg/d) + propranolol(10ng/kg/d) (8)denudation+ phentolamine+ propranolol + immobilization. The serum concentration of END was almost doubled (20pg/ml) by the immobilization stress. The area-ratio (R) of intima/media 14 days thereafter was examined. R was significantly reduced by immobilization (-62%:(2)vs(1)) and was completely restored by NAL (ns:(4)vs(1)). NAL itself had no significant influences (ns:(3)vs(1)). To the contrary, END reduced R (-70%:(5)vs(1)) and was also restored by NAL (ns:(6)vs(1)). Pharmacological blockade of sympathetic activity had little effects (ns:(7)vs(1)) and even under these blockades immobilization significantly reduced R (-59%:(8)vs(7)). The proliferating activity of the medial smooth muscle cells (SMC) assessed by PCNA immunohistochemistly 3 days after denudation showed the parallel results with the neointima formation. The migrating activity for the serum of medial SMC assessed by modified Boyden's chamber method in was also reduced by END (-26%) and completely restored with NAL. **Conclusion** These results indicate that mental stress stimulates the release of endogenous END, which inhibits the intimal fibromuscular proliferation by preventing both proliferation and migration of the medial SMC through opioid receptor. This mechanism may weaken the fibrous cap and make it easy to break.

1179-148 **Is a Radial-Aortic Transfer Function for Total Arterial Compliance Robust in Women and the Elderly?**

Brian A. Haluska, Leanne Short, Phillip Mottram, Stephane G. Carlier, Thomas H. Marwick, University of Queensland, Brisbane, Australia, OLV Hospital, Aalst, Belgium

**Background:** Estimates of central aortic pulse pressure for total arterial compliance (TAC) are based on a radial-aortic transfer function to calculate central pressure from radial applanation tonometry. However, this approach has been validated in groups with a preponderance of middle-aged men, and its validity in women and older patients has been questioned.

**Methods:** Carotid and radial applanation tonometry were performed simultaneously with pulsed wave Doppler of the LVOT using specialised software, in 96 pts (47 men; age 56±8y) with and without cardiovascular disease. TAC was calculated by the pulse-pressure method. Mean aortic pulse pressure (MAoP) was derived using a transfer function from radial tonometry, and then compared with the carotid waveform.

**Results:** The correlation between direct carotid measurement and radial measurement with the transfer function was good for TAC (r= .91). However, there was a significant difference in TAC in older patients (>65 years) using the two waveforms. Bland-Altman analysis of the difference (DIFF) between radial and carotid TAC showed significant differences between men and women (p=0.006) and between younger and older patients (p=0.05) (Table).